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Original

Association of serum vitamin D levels with diabetes mellitus and obesity; a prospective case-control study

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Abstract

Introduction: Vitamin D deficiency has been implicated as a potential risk factor for metabolic disorders, including diabetes mellitus and obesity. Understanding the association between serum vitamin D levels and these conditions could guide future preventive strategies.

Objectives: This study aims to investigate the relationship between serum vitamin D concentrations and the presence of diabetes mellitus and obesity through a prospective case-control design.

Patients and Methods: This prospective case-control study was conducted over three months in Misan province, Iraq, involving 60 women aged 30–40 years, divided equally into healthy controls, obese, and type 2 diabetic groups. Blood samples were collected on the 10th day of the menstrual cycle and analyzed for serum 25-hydroxyvitamin D using an automated immunoassay. The study aimed primarily to compare vitamin D levels across the groups and secondarily to explore the relationship between vitamin D status and the presence of obesity and diabetes.

Results: The comparative analysis of serum vitamin D levels among healthy individuals, obese individuals, and diabetes patients revealed a highly significant overall difference, with both the obese individuals and diabetic patients exhibiting notably lower vitamin D concentrations than healthy individuals. However, no significant difference was found between the vitamin D levels of obese and diabetic individuals, indicating comparable deficiencies in these metabolic disorder populations.

Conclusion: The study identified a significant negative association between vitamin D concentration and both obesity and diabetes, highlighting the importance of targeted screening for metabolic disorders and vitamin D deficiency.

Keywords: Diabetes mellitus, Type 2 diabetes, Obesity, Metabolic diseases, Vitamin D, 25-hydroxyvitamin D, Vitamin D deficiency

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Introduction

Vitamin D deficiency is increasingly recognized as a modifiable factor in the pathogenesis of type 2 diabetes mellitus. Previous studies have indicated that daily intakes exceeding 500 IU and circulating 25-hydroxyvitamin D concentrations above 75 nmol/L are associated with a 13%–43% reduction in the incidence of diabetes (1). Mechanistic studies reveal that inadequate vitamin D impairs pancreatic β-cell function, augments low-grade inflammation, and disrupts calcium and reactive oxygen species signaling, ultimately leading to insulin resistance and β-cell apoptosis (2,3). Meta-analysis studies further demonstrate that short-term, high-dose supplementation can lower fasting glucose, HbA1c, and homeostatic model assessment of insulin resistance (HOMA-IR), particularly among patients with baseline deficiency and elevated body mass index (4).

Obesity is linked to a notable disruption in the secretion of cytokines, which serves as a key indicator for the onset of insulin resistance and the progression to type 2 diabetes (5). This metabolic disorder affects more than one-third of adults worldwide, is consistently linked to lower vitamin D status across age groups and ethnicities (6). Hypovitaminosis D in obesity is attributed to volumetric dilution within expanded adipose, hepatic, and muscular compartments as well as sequestration of the fat-soluble vitamin inside adipocytes (7,8). Meta-analytic evidence shows that excess adiposity not only predicts lower baseline 25-hydroxyvitamin D but also blunts the response to oral supplementation, reducing the post-intervention increment by approximately 38 nmol/L compared with normal-weight controls (9). These observations suggest a bidirectional relationship in which obesity exacerbates vitamin D deficiency, while inadequate vitamin D may, in turn, influence adipose tissue biology and metabolic homeostasis.

Given that both diabetes mellitus and obesity frequently coexist and share vitamin D deficiency as a common, potentially correctable denominator, clarifying their interrelationships is of clinical importance. Emerging data

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Implication for health policy/practice/research/medical education

This study demonstrated a notable inverse relationship between vitamin D levels and the presence of obesity and diabetes, emphasizing the crucial interplay between metabolic health and vitamin D status. These results point out the necessity for targeted screening and intervention efforts, suggesting that addressing vitamin D deficiency could enhance the prevention and management of these metabolic disorders.

indicate that improving vitamin D status can attenuate insulin resistance in pre-diabetes, augment the efficacy of anti-diabetic therapy, and modulate adipokine profiles and inflammatory pathways (10,11). Nevertheless, heterogeneity in study designs, supplementation regimens, and baseline nutritional states has produced conflicting results, underscoring the need for well-designed prospective investigations. The present case-control study, therefore, aims to delineate the association between serum vitamin D levels, diabetes mellitus, and obesity, thereby providing evidence to guide targeted nutritional interventions and public-health strategies.

Objectives

The objective of this prospective case-control study was to investigate the association between serum vitamin D levels and the presence of diabetes mellitus and obesity. Specifically, the study aimed to compare vitamin D concentrations among healthy individuals, obese individuals, and patients with diabetes, in order to determine whether significant differences exist between these groups. By elucidating the relationship between vitamin D status and these metabolic disorders, the study sought to provide evidence supporting the need for targeted screening and interventions to address potential vitamin D deficiency as a contributing factor in obesity and diabetes management.

Patients and Methods

Study design and participants

This prospective case-control study was carried out across several health centers located at Misan province, Iraq, over three months from December 28, 2023 to February 30, 2024. The study population consisted of a total of 60 female participants, aged between 30 and 40 years. These participants were systematically categorized into three equal groups, each comprising 20 women: a healthy control group with no metabolic disorders, an obese group defined by a body mass index (BMI) of 30 kg/m^2 or higher, and a diabetic group consisting of individuals diagnosed with type 2 diabetes mellitus according to established clinical criteria. Participants within three subgroups became age-matched.

Inclusion criteria

The healthy control group included individuals with no prior diagnosis or clinical signs of metabolic disorders, characterized by normal fasting blood glucose levels and a BMI below 25 kg/m^2. The obese group consisted of participants with a BMI of 30 kg/m^2 or higher, without a prior diagnosis of diabetes or other metabolic diseases. The diabetic group included individuals diagnosed with type 2 diabetes mellitus according to American Diabetes Association (ADA) criteria, defined as fasting plasma glucose of 126 mg/dL or higher or HbA1c of 6.5% or above, with or without obesity. All participants were required to provide informed consent and demonstrate willingness to comply with the study protocols.

Exclusion criteria

Individuals with chronic illnesses affecting vitamin D metabolism, such as chronic kidney disease, and the use of medications known to influence vitamin D levels or metabolism, such as vitamin D supplements, corticosteroids, anticonvulsants, or calcium supplements, within the last three months were excluded. Additionally, individuals with irregular or excessive sun exposure due to occupational or lifestyle factors that could bias vitamin D status, as well as those unable or unwilling to provide informed consent or comply with the study protocol, were excluded from participation.

Data collection

At the outset, informed written consent was obtained from all participants, followed by the collection of demographic data through direct interviews. Venous blood samples, ranging from 8 to 10 milliliters, were drawn between 9 and 11 a.m. on the 10th day of each woman's menstrual cycle. Serum vitamin D levels were precisely measured using the VIDAS automated immunoassay system (BioMérieux, France) with the human 25-hydroxyvitamin D [25(OH) D] assay.

Outcomes

The primary outcome of this study is to compare serum vitamin D concentrations among the three groups of healthy individuals, diabetic patients, and individuals with obesity. The secondary outcome focuses on evaluating the association between serum vitamin D concentration and the presence of diabetes mellitus and obesity, to further elucidate the impact of vitamin D deficiency on metabolic health.

Statistical analysis

Statistical Package for Social Sciences (SPSS; IBM Corp., Armonk, NY, USA) was used for data analysis. Data normality was assessed with the Shapiro–Wilk test. Although both parametric and non-parametric approaches were evaluated and yielded comparable P-values, parametric tests were chosen for their superior accuracy and robustness in hypothesis testing. Group differences were analyzed with one-way ANOVA,

followed by least significant difference (LSD) post hoc comparisons. Statistical significance was set at $P < 0.05$ for all tests.

Results

Comparative analysis of serum vitamin D concentrations revealed a highly significant overall difference among the three study populations, including healthy individuals, individuals with obesity, and patients with diabetes mellitus. The analysis reveals that healthy individuals have significantly higher serum vitamin D levels compared to both obese individuals and diabetes patients. However, there is no significant difference in vitamin D levels between obese individuals and those with diabetes. Statistical testing confirms that the differences in vitamin D levels between healthy individuals and the other two groups are highly significant. In contrast, the vitamin D levels of the obese and diabetic groups are comparable. This suggests that both obesity and diabetes are associated with similarly lower vitamin D concentrations relative to healthy controls (Table 1 and Figure 1).

Linear regression analysis examining the correlation of vitamin D levels with metabolic conditions revealed significant negative associations for both diabetes patients and obese individuals when compared to healthy individuals. Obese individuals demonstrated a statistically stronger inverse relationship with serum vitamin D concentrations relative to the healthy reference group, while diabetes patients also exhibited a significant but comparatively moderate negative correlation. The findings indicate that obesity manifests a more pronounced vitamin D deficit compared to diabetes when controlling for baseline healthy population levels, suggesting differential mechanisms or severity of vitamin D dysregulation between these two metabolic conditions (Table 2).

Discussion

Our study found a significant negative correlation between vitamin D levels and both obesity and diabetes; diabetic patients and obese individuals showed lower levels of vitamin D compared to healthy individuals. Previous studies corroborate our finding that lower 25-hydroxy-vitamin D concentrations accompany excess adiposity and impaired glucose metabolism. Some studies of obese adults confirm an inverse dose-response between BMI and vitamin D status (12,13). Similarly, a study demonstrated that lower vitamin D levels were associated with a higher likelihood of developing abdominal obesity (14), while adult observational syntheses have reproduced the same negative gradient across waist-to-hip ratio and total fat mass (15). Parallel evidence exists for type 2 diabetes: an umbrella meta-analysis demonstrated that vitamin-D–deficient cohorts face a 34% higher risk of incident disease (16), and three placebo-controlled trials pooled in a patient-level meta-analysis showed that repletion with 4000 IU/d or equivalent lowered diabetes conversion in pre-diabetes by 15% over three years (17).

Collectively, these data suggest shared physiological pathways whereby excess adiposity sequesters the fat-soluble secosteroid in enlarged adipocytes, accelerates its metabolic clearance, and downregulates hepatic 25-hydroxylase expression, thereby driving systemic insufficiency (18,19). Hypovitaminosis D may, in turn, exacerbate obesity and dysglycemia by dampening insulin receptor expression, impairing β-cell calcium flux, heightening chronic inflammation, and promoting renin–angiotensin activation—mechanisms consistently identified in human and animal studies (20,21). Intervention trials indicate that the magnitude of metabolic benefit is contingent upon achieving serum 25-hydroxy-vitamin D concentrations ≥ 40–50 ng/mL, higher baseline deficiency, and the use of short-term

Table 1. Comparison of age and serum vitamin D levels among diabetes mellitus patients, healthy Individuals, and individuals with obesity

	Group		**Mean**	**SD**	***P* value***
Age (year)	Healthy individuals		34.30	2.29	
	Obese individuals		33.80	2.48	0.177
	Diabetes patients		35.15	2.05	
	Group		**Mean difference**		***P* value****
	Healthy individuals	Obese individuals	0.50		0.492
		Diabetes patients	0.85		0.245
	Obese individuals	Diabetes patients	1.35		0.067
	Group		**Mean**	**SD**	***P* value***
Vit D (ng/ml)	Healthy individuals		35.85	4.65	
	Obese individuals		9.52	1.81	<0.001
	Diabetes patients		9.68	1.85	
	Group		**Mean difference**		***P* value****
	Healthy individuals	Obese individuals	26.32		<0.001
		Diabetes patients	26.17		<0.001
	Obese individuals	Diabetes patients	0.15		0.874

Vit D: Vitamin D, SD: Standard deviation. *ANOVA, **Post hoc LSD.

Figure 1. Comparison of serum vitamin D concentration among healthy individuals, obese Individuals, and diabetes patients using a boxplot chart.

high-dose loading followed by maintenance dosing (22). Nonetheless, heterogeneity in ethnicity, latitude, and assay methodology, together with null findings in some randomized studies, underscores the likelihood of residual confounding and gene–environment interactions (e.g., VDR polymorphisms) that modulate individual responsiveness to supplementation (23).

Over all, our observation of significantly lower vitamin D levels in obese and diabetic participants aligns with a substantial body of evidence spanning epidemiology, mechanistic biology, and clinical trials, reinforcing vitamin D insufficiency as both a marker and potential mediator of metabolic risk. While causality cannot be definitively established, converging data support targeted screening and correction of deficiency, particularly in high-risk, high-BMI or pre-diabetic populations, as a low-cost adjunct to lifestyle and pharmacologic interventions. Future multicenter trials with genotype stratification and harmonized vitamin D assays are warranted to delineate optimal dosing strategies, clarify long-term cardio-metabolic outcomes, and address remaining uncertainties regarding the bidirectional relationship between vitamin D homeostasis, adiposity, and glucose regulation.

Conclusion

This study found a significant negative association between vitamin D levels and the presence of both obesity and diabetes. This finding underscores a critical relationship between metabolic disorders and vitamin D status, highlighting the importance of targeted screening and intervention. Addressing vitamin D deficiency could play a meaningful role in the management and prevention of obesity and diabetes, supporting more effective healthcare strategies for individuals at risk.

Limitations of the study

This study has several limitations that should be considered when interpreting the findings. First, the relatively small sample size of 60 participants, all of whom were women aged 30 to 40 from a single geographical region, limits the generalizability of the results to other populations, including males and other age groups. Second, the cross-sectional nature of the measurements at a single time point does not allow for assessment of causality between vitamin D levels and the development or progression of diabetes and obesity. Third, potential confounding factors such as dietary vitamin D intake, physical activity levels, socioeconomic status, and seasonal variations in sun exposure were not controlled for or reported, which may influence serum vitamin D concentration. Additionally, although exclusion criteria addressed some conditions and medications affecting vitamin D metabolism, subclinical illnesses or unreported supplement use might have influenced the vitamin D status of participants. Future studies with larger, more diverse populations and longitudinal designs are warranted to clarify these associations further.

Table 2. Correlation of vitamin D levels with diabetes and obesity using linear regression compared to healthy individuals

Population	Vitamin D (ng/mL)				
	Unstandardized Coefficients		*P* value	95% CI	
	B	Std. error		Lower	Upper
Obese individuals	-26.32	1.118	<0.001	-28.58	-24.06
Diabetes patients	-13.08	0.561	<0.001	-14.22	-11.95

Authors' contribution

Conceptualization: Farah Kadhim Alwan.
Data curation: Ahmed Aboud Khalifa.
Formal analysis: Ahmed Aboud Khalifa.
Investigation: Farah Kadhim Alwan.
Methodology: Farah Kadhim Alwan and Ahmed Aboud Khalifa.
Project management: Farah Kadhim Alwan.
Resources: Farah Kadhim Alwan and Ahmed Aboud Khalifa.
Supervision: Farah Kadhim Alwan and Ahmed Aboud Khalifa.
Validation: Ahmed Aboud Khalifa.
Writing–original draft: Farah Kadhim Alwan and Ahmed Aboud Khalifa.
Writing–review and editing: Farah Kadhim Alwan and Ahmed Aboud Khalifa.

Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI (Perplexity.ai and Grammarly.com) to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

The study was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from all participants. This research was registered under number (No. 0611514) on December 24, 2023, and approved by the Misan Health Directorate, Training and Human Development Center, University of Misan, Iraq. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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